Contains Nonbinding Recommendations

Draft Guidance on Pregabalin

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active ingredient: Pregabalin

Form/Route: Capsule/Oral

Recommended studies: **2 Options: BCS or In-Vivo Studies**

I. BCS Waiver option:

It may be possible to request a waiver of in-vivo testing for all the strengths of this product provided that the appropriate documentation regarding high solubility, high permeability and rapid dissolution as detailed in the Guidance for Industry: *Waiver of In Vivo Bioavailability and Bioequivalence for Immediate – Release Solid Oral Dosage Forms Based on the Biopharmaceutics Classification System* is submitted in the application. You may use information contained in the approved labeling of the reference product. Peer reviewed articles may not contain the necessary details of the testing for the Agency to make a judgment regarding the quality of the studies. A decision regarding the acceptability of the waiver request can only be made upon review of the data submitted in the application.

II. In-Vivo option:

1. Type of study: Fasting
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 300 mg
   Healthy males and nonpregnant females, general population
   Additional Comments: Pregabalin has been associated with birth defects in animal studies. Therefore, women of childbearing potential should be excluded from in-vivo bioequivalence studies of this product. Participants should be provided with the information in the patient information leaflet for the RLD, and male subjects should agree to use condoms during sexual intercourse with a woman of childbearing potential while participating in the BE study and for at least 10 weeks (one complete sperm cycle) after the last dose of study drug.

---

2. Type of study: Fed
   Design: single-dose, two-way crossover *in-vivo*
   Strength: 300 mg
   Subjects: Normal healthy males and females, general population.
   Additional comments: Please see above comment

Analytes to measure: Pregabalin in plasma

Bioequivalence based on (90% CI): Pregabalin

Waiver request of in-vivo testing: 25, 50, 75, 100, 150, 200, 225 mg based on (i) acceptable bioequivalence studies on the 300 mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

Dissolution test method and sampling times:

Please note that a **Dissolution Methods Database** is available to the public at the OGD website at http://www.fda.gov/cder/ogd/index.htm. Please find the dissolution information for this product at this website. Please conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the application.